

APR 12 2004 Attorney Docket No. RADO-001/02US

PATENT

BY PATENT & TRADEMARKS I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to the Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on April 8, 2004.

By:

*Cathi L.G. Thoorsell*

Cathi L.G. Thoorsell

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of Mark D. BEDNARSKI *et al.*

Serial No.: 10/681,855 Examiner: Not yet assigned

Confirmation No.: 7135 Art Unit: 1614

Filed: October 7, 2003

For: **X-NITRO COMPOUNDS, PHARMACEUTICAL COMPOSITIONS THEREOF AND USES THEREOF**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

### INFORMATION DISCLOSURE STATEMENT TRANSMITTAL

Enclosed is an Information Disclosure Statement and accompanying Form PTO/SB/08A for the above-identified patent application. In accordance with 37 C.F.R. §1.97(b), no additional fee for submission of the IDS is required. A return receipt postcard is also enclosed.

The Commissioner is hereby authorized to charge any appropriate fees under 37 C.F.R. §§1.16, 1.17, and 1.21 that may be required by this paper, and to credit any overpayment, to Deposit Account No. 03-3117.

Dated: April 8, 2004

Cooley Godward LLP  
ATTN: Patent Group  
Five Palo Alto Square  
3000 El Camino Real  
Palo Alto, CA 94306-2155  
Tel: (650) 843-5000 Fax: (650) 857-0663  
672394 v1/PA

Respectfully submitted,  
**COOLEY GODWARD LLP**

By:

*Sunil K. Singh*  
Sunil K. Singh  
Reg. No. 45,298

Attorney Docket No. RADO-001/02US

PATENT



I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to the Commissioner for Patents, P.O. Box 3450, Alexandria, VA 22313-1450 on April 8, 2004.

By:

Cathi L.G. Thoressell  
Cathi L.G. Thoressell

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of Mark D. BEDNARSKI *et al.*

Serial No.: 10/681,855 Examiner: Not yet assigned

Confirmation No.: 7135 Art Unit: 1614

Filed: October 7, 2003

For: **X-NITRO COMPOUNDS, PHARMACEUTICAL COMPOSITIONS  
THEREOF AND USES THEREOF**

---

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

### INFORMATION DISCLOSURE STATEMENT UNDER 37 C.F.R. §1.97(b)

In accordance with the duty of disclosure set forth in 37 C.F.R. §1.56, Applicant(s) hereby submits the following information in conformance with 37 C.F.R. §§1.97 and 1.98. Pursuant to 37 C.F.R. §1.98, a copy of each document cited in the attached Form PTO/SB/08 is enclosed. This Information Disclosure Statement is filed before the mailing date of a first office action on the merits.

It is respectfully requested that the Examiner consider the above-noted information and return an initialed copy of the attached Form PTO/SB/08A to the undersigned.

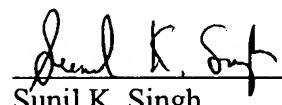
Dated: April 8, 2004

Cooley Godward LLP  
ATTN: Patent Group  
Five Palo Alto Square  
3000 El Camino Real  
Palo Alto, CA 94306-2155  
Tel: (650) 843-5000  
Fax: (650) 857-0663

672395 v1/PA

Respectfully submitted,  
**COOLEY GODWARD LLP**

By:

  
Sunil K. Singh

Reg. No. 45,298

Please type a plus sign (+) inside this  box →

PTO/SB/08A (08-00)



|                                                                                                                                   |   |    |   |                          |                   |
|-----------------------------------------------------------------------------------------------------------------------------------|---|----|---|--------------------------|-------------------|
| Substitute for form 1449A/PTO<br><b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b><br><i>(use as many sheets as necessary)</i> |   |    |   | <i>Complete if Known</i> |                   |
|                                                                                                                                   |   |    |   | Application Number       | 10/681,855        |
|                                                                                                                                   |   |    |   | Filing Date              | October 7, 2003   |
|                                                                                                                                   |   |    |   | First Named Inventor     | Mark D. BEDNARSKI |
|                                                                                                                                   |   |    |   | Group Art Unit           | 1614              |
|                                                                                                                                   |   |    |   | Examiner Name            | not yet assigned  |
| Sheet                                                                                                                             | 1 | of | 3 | Attorney Docket Number   | RADO-001/02US     |

| <b>U.S. PATENT DOCUMENTS</b> |                       |                      |            |                                                 |                                                  |
|------------------------------|-----------------------|----------------------|------------|-------------------------------------------------|--------------------------------------------------|
| Examiner Initials*           | Cite No. <sup>1</sup> | U.S. Patent Document |            | Name of Patentee or Applicant of Cited Document | Date of Publication of Cited Document MM-DD-YYYY |
|                              |                       | Number               | (if known) |                                                 |                                                  |
| P1                           | 5,970,974             |                      |            | Van Der Linden, Klaus                           | 10-26-1999                                       |
| P2                           | 5,954,047             |                      |            | Armer, Thomas Alex                              | 09-21-1999                                       |
| P3                           | 5,950,619             |                      |            | van der Linden, Klaus                           | 09-14-1999                                       |
| P4                           | 5,698,155             |                      |            | Grosswald, Ralph R.                             | 12-16-1997                                       |
| P5                           | 5,579,458             |                      |            | Yokosuka, Hirobumi                              | 11-26-1996                                       |
| P6                           | 5,556,611             |                      |            | Biesalski, Hans K                               | 09-17-1996                                       |
| P7                           | 5,112,598             |                      |            | Biesalski, Hans K.                              | 05-12-1992                                       |
| P8                           | 4,765,539             |                      |            | Noakes, Timothy J.                              | 08-23-1988                                       |
| P9                           | 3,916,899             |                      |            | Theeuwes, Felix                                 | 11-04-1975                                       |
| P10                          | 3,845,770             |                      |            | Theeuwes, Felix                                 | 11-05-1974                                       |

| <b>FOREIGN PATENT DOCUMENTS</b> |                       |                                          |                     |                    |                                                  |
|---------------------------------|-----------------------|------------------------------------------|---------------------|--------------------|--------------------------------------------------|
| Examiner Initials*              | Cite No. <sup>1</sup> | Foreign Patent Document                  |                     |                    | Date of Publication of Cited Document MM-DD-YYYY |
|                                 |                       | Office <sup>3</sup><br>Code <sup>5</sup> | Number <sup>4</sup> | Kind<br>(if known) |                                                  |
|                                 |                       |                                          |                     |                    |                                                  |
|                                 |                       |                                          |                     |                    |                                                  |
|                                 |                       |                                          |                     |                    |                                                  |
|                                 |                       |                                          |                     |                    |                                                  |
|                                 |                       |                                          |                     |                    |                                                  |
|                                 |                       |                                          |                     |                    |                                                  |

|                    |                 |
|--------------------|-----------------|
| Examiner Signature | Date Considered |
|--------------------|-----------------|

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Unique citation designation number.

<sup>2</sup> See attached Kinds of U.S. Patent Documents.

<sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3).

<sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document.

<sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible.

<sup>6</sup> Applicant is to place a check mark here if English language Translation is attached.

Please type a plus sign (+) inside this box →

PTO/SB/08A (08-00)

|                                                                                                                                   |                   |    |   |                          |                   |
|-----------------------------------------------------------------------------------------------------------------------------------|-------------------|----|---|--------------------------|-------------------|
| Substitute for form 1449B/PTO<br><b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b><br><i>(use as many sheets as necessary)</i> |                   |    |   | <i>Complete if Known</i> |                   |
|                                                                                                                                   |                   |    |   | Application Number       | 10/681,855        |
|                                                                                                                                   |                   |    |   | Filing Date              | 10/07/2003        |
|                                                                                                                                   |                   |    |   | First Named Inventor     | Mark D. BEDNARSKI |
|                                                                                                                                   |                   |    |   | Group Art Unit           | 1614              |
| Examiner Name                                                                                                                     | Not yet assigned. |    |   |                          |                   |
| Sheet                                                                                                                             | 2                 | Of | 3 | Attorney Docket Number   | RADO-001/02US     |

| <b>OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS</b> |          |                                                                                                                                                                                                                                                                 |  |  |                |
|----------------------------------------------------------|----------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|--|----------------|
| Examiner Initials*                                       | Cite No. | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published. |  |  | T <sup>2</sup> |
|                                                          | D1       | <u>ALDERMAN, A. "A Review of Cellulose Ethers in Hydrophilic Matrices for Oral Controlled-Release Dosage Forms,"</u> <i>Int. J. Pharm. Tech &amp; Prod. Mfr.</i> (1984) 5(3) 1-9.                                                                               |  |  |                |
|                                                          | D2       | <u>ARMSTRONG et al., "Role of Glutathione Depletion and Reactive Oxygen Species Generation in Apoptotic Signaling in a Human B Lymphoma cell line,"</u> <i>Cell Death Differ.</i> (2002) 9(3); 252-263.                                                         |  |  |                |
|                                                          | D3       | <u>BAMBA et al., "Release Mechanisms In Gelforming Sustained Release Preparation,"</u> <i>Int. J. Pharm.</i> (1979), 2, 307.                                                                                                                                    |  |  |                |
|                                                          | D4       | <u>BERGE et al., "Pharmaceutical Salts,"</u> <i>J. Pharm. Sci.</i> (1977) 66:1-19.                                                                                                                                                                              |  |  |                |
|                                                          | D5       | <u>BROWN et al. Tirapazamine: Laboratory Data Relevant to Clinical Activity Anti-cancer Drug Design</u> (1998), 13, 529-539.                                                                                                                                    |  |  |                |
|                                                          | D6       | <u>DURING et al. "Controlled Release of Dopamine from a Polymeric Brain Implant: In Vivo Characterization,"</u> <i>Ann. Neurol.</i> (1989) 25:351.                                                                                                              |  |  |                |
|                                                          | D7       | <u>HOWARD et al., "Intracerebral Drug Delivery in Rats with Lesion-induced Memory Deficits,"</u> <i>J. Neurosurg.</i> (1989) 71:105.                                                                                                                            |  |  |                |
|                                                          | D8       | <u>LANGER (1990) "New Methods of Drug Delivery,"</u> <i>Science</i> 249: 1527-1533                                                                                                                                                                              |  |  |                |
|                                                          | D9       | <u>LANGER "Chemical and Physical Structure of Polymers as Carriers for Controlled Release of Bioactive Agents: a Review"</u> <i>JMS-Rev. Macromol. Chem. Phys</i> (1983) C23(1), 61-126.                                                                        |  |  |                |
|                                                          | D10      | <u>LEVY et al. "Inhibition of Calcification of Bioprosthetic Heart Valves by Local Controlled-Release Diphosphonate,"</u> <i>Science</i> (1985) 228:190-196.                                                                                                    |  |  |                |
|                                                          | D11      | <u>NING et al. "The Antiangiogenic Agents SU5416 and SU 6668 Increase the Antitumor Effects of Fractionated Irradiation,"</u> <i>Radiat. Res.</i> (2002) 157(1): 45-51.                                                                                         |  |  |                |
|                                                          | D12      | <u>ROSENTHAL et al., "A Phase I Single-Dose Trial of Gadolinium Texaphyrin (Gd-Tex), a Tumor Selective Radiation Sensitizer Detectable by Magnetic Resonance Imaging,"</u> <i>Clin. Cancer Res.</i> , (1999), 739-745.                                          |  |  |                |
|                                                          | D13      | <u>RUPNOW et al., "p53 Mediates Apoptosis Induced by c-Myc Activation in Hypoxic or Gamma Irradiated Fibroblasts,"</u> <i>Cell Death Differ.</i> (1998) 5(2): 141-147.                                                                                          |  |  |                |

|                                                                                                                                           |   |    |   |                               |                   |
|-------------------------------------------------------------------------------------------------------------------------------------------|---|----|---|-------------------------------|-------------------|
| <p>Substitute for form 1449B/PTO</p> <p><b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b></p> <p>(use as many sheets as necessary)</p> |   |    |   | <i>Complete if Known</i>      |                   |
|                                                                                                                                           |   |    |   | <b>Application Number</b>     | 10/681,855        |
|                                                                                                                                           |   |    |   | <b>Filing Date</b>            | 10/07/2003        |
|                                                                                                                                           |   |    |   | <b>First Named Inventor</b>   | Mark D. BEDNARSKI |
|                                                                                                                                           |   |    |   | <b>Group Art Unit</b>         | 1614              |
|                                                                                                                                           |   |    |   | <b>Examiner Name</b>          | Not yet assigned. |
| Sheet                                                                                                                                     | 3 | Of | 3 | <b>Attorney Docket Number</b> | RADO-001/02US     |

|  |     |                                                                                                                                                                                             |  |
|--|-----|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|
|  | D14 | SAUDEK <i>et al.</i> , "A Preliminary Trial of the Programmable Implantable Medication System for Insulin Delivery," <i>N. Engl. J. Med.</i> (1989) 321:574-579.                            |  |
|  | D15 | SEFTON, "Implantable Pumps," <i>CRC Crit. Ref. Biomed. Eng.</i> (1987) 14:201-240.                                                                                                          |  |
|  | D16 | STRATFORD <i>et al.</i> <u>Bioreductive Drugs into the Next Millennium Anti-Cancer Drug Design</u> (1998), 13, 519-528.                                                                     |  |
|  | D17 | TREAT <i>et al.</i> , "Liposomes in the Therapy of Infectious Disease and Cancer" Lopez-Berestein and Fidler (eds.), Liss, New York (1989), pp. 353-365.                                    |  |
|  | D18 | VERMA <i>et al.</i> , "Osmotically Controlled Oral Drug Delivery" <i>Drug Dev. Ind. Pharm.</i> , (2000), 26:695-708.                                                                        |  |
|  | D19 | VERSCHOYLE <i>et al.</i> , "Pharmacokinetics of Isotretinoin (ISO) in Rats Following Oral Dosing or Aerosol Inhalation," <i>British J. Cancer</i> , 1999, 80, Suppl. 2, 96.                 |  |
|  | D20 | WILSON, <i>et al.</i> <u>Radiation-activated Prodrugs as Hypoxia-selective Cytotoxins: Model Studies with Nitroaryl methyl Quaternary Salts Anti-cancer Drug Design</u> (1998) 13, 663-685. |  |
|  | D21 | YAMAGUCHI <i>et al.</i> <u>Protodynamic Therapy with Motexafin Lutetium (Lu-Tex) Reduces Experimental Graft Coronary Artery Disease Transplantation</u> (2001) June 15:71(11) 1526-32.      |  |

|                    |  |                 |  |
|--------------------|--|-----------------|--|
| Examiner Signature |  | Date Considered |  |
|--------------------|--|-----------------|--|

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

672396 v1/PA

<sup>1</sup> Unique citation designation number.

<sup>2</sup> Applicant is to place a check mark here if English language Translation attached.